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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/666,430	09/21/00	REA	D 4205.1US

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1644	6

DATE MAILED: 06/29/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/666,430	Rea et al
Examiner	**Art Unit**
F. Pierre VanderVegt	1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Apr 19, 2001*

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1, 4-15, 17-19, and 28-36* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideratio

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1, 4-15, 17-19, and 28-36* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

This application claims priority to provisional application 60/157,442.

Claims 16, 20, 22 and 24-27 have been canceled. New claims 30-36 have been added.

Claims 1, 4-15, 17-19 and 28-36 are currently pending in this application.

Election/Restriction

1. Applicant's election without traverse of Group I, claims 1, 4-15, 17-19 and 28-29, in Paper No. 5, filed April 19, 2001, is acknowledged. New claims 30-36 are commensurate with the elected invention and will be examined therewith. Applicant's cancellation of all non-elected claims without disclaimer is noted.

Specification

2. The disclosure is objected to because of the following informalities: .

35 U.S.C. 112, first paragraph, requires the specification to be written in "full, clear, concise, and exact terms." The specification is replete with terms which are not clear, concise and exact. The specification should be revised carefully in order to comply with 35 U.S.C. 112, first paragraph. Examples of some unclear, inexact or verbose terms used in the specification are: at page 2, lines 29-31, "...but that it converts CD40 ligation on human monocyte-derived DC is transformed into an alternative activation pathway..." and "DEX profoundly affect the CD40-dependent maturation..." (page 2, lines 31-32) as well as misspellings such as "dentritic" and "posses" (both at page 4, line 23).

Appropriate correction is required.

Claim Rejections - 35 U.S.C. § 112

3. Claims 1, 4-15 and 28-36 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to the generation of dendritic cells (DCs) from monocytes, treatment of the dendritic cells with glucocorticoid (GC), incubation of the GC-treated DCs with antigen, and incubating the DCs with T cells to ablate an unwanted T cell response. However, the instant specification as filed fails to provide descriptive support for any GC other than dexamethasone. Beyond generic statements throughout the specification mentioning the effect of "glucocorticoid" on dendritic cells, Applicant has not disclosed or exemplified glucocorticoids other than dexamethasone.

Vas-Cath Inc. v. Mahurkar ((CAFC, 1991) 19 USPQ2d 1111), clearly states that "Applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See *Vas-Cath* at page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

The Courts have further ruled that, "Entitlement to a filing date does not extend to subject matter which is not disclosed, but would be obvious over what is expressly disclosed" (*Lockwood v. American Airlines Inc.* 107 F.3d 1565, 41 U.S.P.Q.2d 1961 (Fed. Cir. 1997)). While other GCs may be obvious over dexamethasone, mere reference to the genus as glucocorticoid or GC does not constitute written descriptive support of the genus over the disclosure that dexamethasone is effective for the practice of the claimed invention.

Accordingly, the written description in this case only sets forth dexamethasone as a suitable GC for the practice of the claimed invention and a single species of GC is not sufficiently descriptive of the entire genus. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see *Vas-Cath* at page 1115).

4. Claims 1, 4-15 and are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the in vitro induction of non-responsiveness of MHC-matched clonal T cells to an defined antigen when dexamethasone-treated dendritic cells have

been loaded with the same defined antigen, does not reasonably provide enablement for in vivo or in vitro induction of non-responsiveness of polyclonal T cells to any undefined antigen or the in vivo induction of non-responsiveness when an "unwanted T-cell response" is ongoing. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are drawn to the generation of dendritic cells (DCs) from monocytes, treatment of the dendritic cells with glucocorticoid (GC), incubation of the GC-treated DCs with antigen, and incubating the DCs with T cells to ablate an unwanted T cell response. However, the enablement provided by the instant specification does not extend beyond the loading of an antigen onto dendritic cells in vitro which is known to be the same antigen with which a clonal line of T cells is reactive. The specification discloses at page 5, lines 19-27, "An antigen typically is a peptide capable of binding to a major histocompatibility complex I and/or II molecule. Such peptides are known in the art and a person skilled in the art is capable of determining whether a given peptide comprises an antigen or not." The specification does not provide any guidance regarding antigens to which an "unwanted T-cell response" may be found. While an artisan may be able to identify MHC bindings antigens in general terms, more specific guidance is required in the identification of those to which an "unwanted T-cell response" may be found. The sole example in the specification discloses the in vitro incubation of dexamethasone-treated dendritic cells with an antigen to which in vitro clonal T cell lines are known to be reactive, incubating in vitro the dendritic cells with said T cells and measuring the response in vitro to that known antigen. The specification repeatedly states that the preferred subject is a patient with or at risk for an autoimmune condition, allergy, graft-versus-host or host-versus-graft disease, for example. However, the specification fails to disclose exemplary antigens which may be useful in the treatment or prevention of the conditions. Further, the claims encompass the treatment of ongoing adverse immune reactivity in a patient and this is not enabled. Focusing on the treatment of an autoimmune disease, it should be noted that the effectiveness of treating a response to an autoantigen is dependent on several factors, the most critical of which is whether the therapy can be used to treat an ongoing autoimmune response or whether it is only effective prophylactically

(Tisch et al, U on form PTO-892, page 437, column 2, last paragraph in particular). Typically, an autoimmune disease is diagnosed only after significant tissue damage has already occurred. Administration of antigen after pathogenic T cells have been activated may have an exacerbating effect on the disease, rather than a tolerogenic one. The same principle applies when administering dendritic cells loaded with a particular antigen. Another problem during the treatment of autoimmune diseases is determinant spreading during the course of the disease. The Tisch et al reference also teaches that "the high degree of specificity required for the process of clonal deletion/anergy may be limiting when dealing with diseases such as MS, IDDM, and RA, in which there are responses to several autoantigens [...] and the critical inciting autoantigen(s) is not known" (page 437, third full paragraph of column 3 in particular). The breadth of Applicant's claims are such that they include treatment of autoimmune diseases with antigens which have not been characterized. The claims confer no degree of specificity with which one of skill in the art could relate the treating antigen with a particular condition. Therefore the art would predict that it would be counterproductive to treat autoimmune disease patients with autoantigen-loaded dendritic cells, as such treatment would more likely than not exacerbate the ongoing immune response. The artisan is not provided sufficient information by the instant specification in order to practice the method of the instant claimed invention over a long-term course for treatment of an ongoing immune response and may result in exacerbation rather than relief.

Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 17-19 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Steptoe et al (V).

The claims are drawn to the alteration of a T cell response to an antigen by incubating the T cell with a dendritic cell. The claims encompass the induction of hyporesponsiveness to an antigen, an alteration of the T cell's normal function of reacting with said antigen. Steptoe et al provides a treatise on the role of dendritic cells in tolerance induction. Steptoe et al teaches that dendritic cells propagated from precursors in vitro with low levels of GM-CSF induce alloantigen-specific unresponsiveness in T cells in vitro. The prior art teaching clearly anticipates the claimed invention.

Conclusion

6. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which Applicant may become aware in the specification.

7. Papers related to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. Papers should be faxed to Group 1640 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The fax phone number for official documents to be entered into the record for Art Unit 1644 is (703)305-3014.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to F. Pierre VanderVegt, whose telephone number is (703)305-6997. The Examiner can normally be reached Tuesday through Friday and odd-numbered Mondays (on year 2001 365-day calender) from 6:30 am to 4:00 pm ET. A message may be left on the Examiner's voice mail service. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ms. Christina Chan can be reached at (703)308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist, whose telephone number is (703)308-0196.

F. Pierre VanderVegt, Ph.D.
Patent Examiner
Technology Center 1600
June 28, 2001

F. PIERRE VANDERVEGT
PATENT EXAMINER